

# **Computerized respiratory sound analysis in people with dementia: a first-step towards diagnosis and monitoring of respiratory conditions**

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## Abstract

Computerized respiratory sound analysis has shown to be objective and reliable to assess respiratory diseases. However its application in non-collaborative populations, as people with dementia, is still unknown. Therefore this study aimed to characterize normal and adventitious respiratory sounds (NRS; ARS) in older people with and without dementia.

A cross-sectional study including two groups of 30 subjects with dementia and 30 subjects without dementia was performed. Digital auscultation was used to record NRS and ARS per breathing-phase (inspiration/expiration) at trachea and thorax. Frequency at percentiles 25, 50 and 75, frequency at maximum-intensity, maximum-intensity (Imax) and mean-intensity (Imean) characterized NRS. Crackles' number, frequency, initial-deflection-width, 2cycle-duration, and largest-deflection-width and wheezes' number, frequency and occupation-rate characterized ARS.

Groups were similar in socio-demographics, except for anthropometrics. No significant differences were found between groups in NRS frequency or ARS at trachea or thorax. Significant lower Imax (inspiration: 36.88[29.42;39.92] vs. 39.84[36.50;44.17]  $p=0.007$ ; expiration: 34.51[32.06;38.87] vs. 42.33[36.92;44.98]  $p<0.001$ ) and Imean (inspiration: 15.23[12.08;18.60] vs. 18.93[15.64;21.82]  $p=0.003$  and expiration: 14.57[12.08;18.30] vs. 18.87[15.64;21.44]  $p=0.001$ ) at trachea and higher Imean (inspiration: 17.29[16.04;19.31] vs. 16.45[15.05; 18.79]  $p=0.005$  and expiration: 16.71[15.31;18.56] vs. 16.38[14.40;17.85]  $p=0.011$ ) at thorax were found in subjects with dementia when compared with subjects without dementia. To conclude people with and without dementia had similar NRS and ARS characteristics, except for NRS intensity. Computerized respiratory sound analysis was feasible in a non-collaborative population. Further research is needed to enhance the use of respiratory acoustics in non-collaborative populations, with strong potential to be applied in different settings for diagnosis and monitoring purposes.

**Keywords:** Digital Auscultation; Normal respiratory sounds; Adventitious respiratory sounds; Older people; Dementia.

## 1. Introduction

Dementia is one of the most common chronic conditions among older people (1). Recent estimates point for a worldwide prevalence of 48.1 million in 2020 and 90.3 million in 2040, which tend to increase with demographic aging (1).

Lower Respiratory Tract Infections (LRTIs) are highly prevalent among people with dementia, being the ultimate cause of mortality in up to 2/3 of this population (2, 3). These infections also intensify cognitive and functional decline, compromise functionality (4) and are one of the main reasons for hospitalization (5), representing an important cause of morbidity, mortality and health costs worldwide. Consequently, a number of attempts and recommendations have been described to prevent and manage LRTIs in people with dementia (6-8). However, assessing the respiratory system of this population has been shown to be highly challenging for mainly two reasons. Firstly, people with dementia constitute a non-collaborative population, and therefore their clinical evaluation is often difficult, mainly in moderate to severe stages, as patients do not complain, follow orders or report reliable information about their health state (9). Then, the lack of accuracy, reliability and sensitivity of most respiratory measures (10), also impairs the assessment of the respiratory system and the comparisons between patients and clinical cases.

Pulmonary auscultation is a non-invasive and economic method to assess the respiratory system and can be applied in all populations and settings (10). No other method provides relevant information about the respiratory system as quickly, easily and by nearly universally available means (11). Therefore, efforts based on computerized techniques have been developed to overcome its main disadvantage, the subjectivity (11). Computerized respiratory sound analysis, which consists of recording patients' respiratory sounds with an electronic device and classifying/analyzing them based on specific signal characteristics, is an objective, simple and non-invasive method to detect and characterize normal respiratory sounds (NRS) and adventitious respiratory sounds (ARS) (12). Previous research has shown that the occurrence of a respiratory condition is often marked by changes in frequency and intensity of NRS (11) and/or presence of ARS (13, 14). Additionally, computerized respiratory sound analysis has shown to be efficient in detecting several respiratory conditions (10, 15-20), even earlier than other measures (21). Studies using this technique have also been conducted in intensive care units (22, 23) or clinical settings after hospital admissions (18) and have demonstrated its applicability to detect and analyze alterations in respiratory sounds and exacerbation states (18, 22, 23).

Therefore, computerized respiratory sounds show potential to support the diagnosis and continuous monitoring of respiratory diseases in different settings and may have an important role in non-collaborative populations. However, its applicability in non-collaborative populations has never been explored. Hence, this study aimed to characterize NRS and ARS in people with dementia living in long-term care homes. It also aimed to compare normal and adventitious respiratory sounds characteristics of people with dementia with an age and gender matched sample of people without dementia living in the same conditions.

## **2. Methods**

### **2.1 Design and Ethics**

A cross-sectional descriptive study was conducted. All procedures were in accordance with the ethical standards of the institutions, national research committee and with the 1964 Helsinki declaration. Ethical approval was previously obtained by an Ethics Committee for Health (Decision number: P72\_02\_2012). Prior to any data collection, written informed consents were collected from autonomous participants or from participants' legal representatives.

### **2.2 Sample**

Six long-term care facilities were contacted and after an arranged meeting to explain the purpose of the study, all agreed to participate. The service managers together with the physician and the nurse identified potential eligible participants and two groups were formed: a group of older people with dementia (DG) and a control group (CG) of older people without dementia.

Subjects with dementia were included if they were 60 years old or older and presented a medical diagnosis of irreversible dementia, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV criteria) (24). Subjects without dementia were included if they were 60 years old or older. Potential participants were excluded from both groups if they: i) presented significant cardiac or respiratory disease medically diagnosed, and/or were prescribed with medication for significant cardiac or respiratory disease; ii) refused to answer to the Mini-Mental State Examination (MMSE); iii) refused respiratory auscultation; iv) were talking, moving up or restless during auscultation; v) and were unable to sign or did not have a legal representative to sign the written informed consent.

### **2.3 Measures**

Socio-demographic and anthropometric data were collected with a structured questionnaire based on the characterization items of the International Classification of Functioning, Disability and Health (ICF) Checklist (25). Socio-demographic data included gender, date of birth, level of education and marital status. Anthropometric data included waist circumference and skin folds.

The Mini-Mental State Examination (MMSE) (26) was applied to assess participants' cognitive status. The MMSE was chosen as it is the most applied cognitive test in people with dementia, is brief, simple and has been adapted to different populations and cultures (27, 28). The scores range from 0 to 30, with lower scores indicating higher cognitive impairment (29).

The Global Deterioration Scale (GDS) (30, 31) was used to characterize the severity of cognitive impairment. This is a brief and simple scale commonly used to differentiate the disease into 7 stages based on the amount of cognitive decline. Stages 1-3 represent no dementia and stages 4-7 indicate dementia (30).

Respiratory sounds were collected with a digital stethoscope (WelchAllyn 5079-400) connected to an external sound card (Cakewalk UA-25EX). The signal was converted with a 24-bit resolution at a sample rate of 44100 samples per second (32) and recorded in a wav. format

on a laptop computer with an interface developed to collect and analyze respiratory sounds (33). Each sound recording was performed during 20 seconds according to the Computerized Respiratory Sound Analysis (CORSAs) guidelines for short-term acquisition (34). All data were collected by the same researcher, who received long-term training from a senior research expert in this field.

## 2.4 Procedures

Socio-demographic and anthropometric data, level of cognition, type and severity of dementia were collected following this order to characterize the sample. These data were fulfilled by the researcher using information from clinical notes, staff (health professionals and service managers) and through individual assessment of each participant.

Respiratory sounds were collected with participants sitting on a chair, wheelchair or bed ensuring a 90° angle between the spinal column and the lower limbs. Seven regions were recorded according to the short-term respiratory sounds acquisition guidelines (34): trachea (laterally on the sternal notch), anterior (at the second intercostal space in mid-clavicular line right and left), lateral (at the fourth or fifth intercostal space on the mid-axillary line right and left) and posterior (5 cm laterally from the paravertebral line and 7 cm below the scapular angle right and left) areas, using reference points to ensure that the stethoscope was placed on the same point in each participant (34). Normal and Adventitious respiratory sounds of the 420 sound files (7 regions from 60 participants) were characterized per breathing phase (i.e., inspiration and expiration), detected manually by the researcher. Then, these areas were grouped into trachea and thorax to facilitate the sound analysis.

Normal respiratory sounds were characterized through the analysis of spectrum parameters: percentile frequencies  $F_{25}$ ,  $F_{50}$ , and  $F_{75}$ , frequency at maximum intensity ( $F_{max}$ ), maximum intensity ( $I_{max}$ ), and mean intensity over the whole frequency range ( $I_{mean}$ ). All parameters were extracted per breathing phase (35). The sound intensities were calculated in dB, and the reference used was the baseline noise of the data acquisition system ( $1.5 \times 10^{-10}$  W). The frequency was analyzed because it provides information about the acoustical properties of trachea and thorax (14). The intensity of NRS was also measured as it has been suggested that a decrease in sound intensity may indicate abnormal characteristics of normal sound (11). Although it is known that normal respiratory sound frequencies can range from 100-5000 Hz at trachea and from 100–1000 Hz at thorax (11), in this study we analyzed the frequency band of 100-2000 Hz, as it includes all range frequencies from the thorax and the majority from the trachea, which presented little energy beyond 1500 Hz (36).

Adventitious respiratory sounds were characterized through the analysis of crackles' number (N), frequency (F), initial deflection width (IDW), two cycle duration (2CD), and largest deflection width (LDW) and wheezes' number (N), frequency (F) and occupation rate (Wh%) per breathing phase at trachea and thorax. The variable number was chosen as the number of crackles usually reflects a pathological process in pulmonary tissue or airways (37, 38). The variable frequency was studied as it allows identification of crackles' source (13, 20). The IDW, 2CD and

LDW were collected because these parameters allow crackle's characterization (13). Both IDW and 2CD have reference values which classify crackles in fine (mean IDW of 0.7ms; 2CD<10 ms) or coarse (mean IDW of 1.5ms; 2CD>10 ms) (38-40). The LDW was studied as it was considered a good parameter to classify crackles (41) for diagnostic purposes (37), or to follow-up pulmonary diseases (19). Additionally, the number of wheezes was analyzed as it provides information on the possible presence of obstructive lung diseases and the degree of bronchial obstruction (42). The fundamental frequency was studied since it provides information on the source of the wheeze (13). The Wh% was examined because the proportion of the respiratory cycle occupied by wheezing is associated with the degree of bronchial obstruction (43).

## **2.5 Data analyzes and statistics**

Data from the structured questionnaire were inserted in a database of the PASW Statistics version 19.0 for Windows (SPSS Inc., Chicago, Illinois). Descriptive statistics were applied to characterize the sample (i.e., socio-demographic and anthropometric data, cognitive status, type and severity of dementia). The two groups' characterization variables were compared using Chi-square tests or Independent samples tests, since they were categorical or numerical variables, respectively.

All sound files were processed using published algorithms written in Matlab2009 (The MathWorks, Inc, Natick, MA, USA). The normal distribution of data was explored with Kolmogorov-Smirnov test (44). Differences between groups were explored with independent t-test for continuous normally distributed data and Mann-Whitney *U*-test for continuous non-normally distributed data (44).

Normal respiratory sound signals power spectrum was estimated via Welch's method adopting 256-point Hamming windows with 50% overlap, and 2<sup>14</sup>-point fast Fourier transformation (35). Descriptive statistics were used to characterize F25, F50, and F75, I<sub>max</sub>, F<sub>max</sub>, and I<sub>mean</sub>. Mann-Whitney *U*-test was applied to compare differences in F25, F50, and F75, I<sub>max</sub>, F<sub>max</sub>, and I<sub>mean</sub> between the groups at trachea and thorax per breathing phase (44).

Crackles were detected automatically using an interface developed by Pinho et al. in 2012 (33), which incorporated an algorithm based on the combination of fractal dimension (45-48), box filtering (49) techniques and the crackle established criteria (13, 50). Descriptive statistics were used to characterize N, *f*, IDW, 2CD, and LDW of crackles per breathing phase at trachea and thorax. Mann-Whitney *U*-test was applied to compare the groups' N, *f*, IDW, 2CD, LDW of crackles at trachea and thorax per breathing phase (44).

Wheezes were also detected automatically with the developed interface (33) using the algorithm developed by Taplidou and Hadjileontiadis (2007) and validated by Oliveira et al. (2011) (52). This algorithm has demonstrated a sensitivity of 99.2%, a specificity of 72.5% and a performance of 84.8% in wheezes' automatic detection (53). Descriptive statistics were used to assess the presence of wheezes in participants' trachea and thorax. Mann-Whitney *U*-test was

applied to compare the wheezes N, *f* and Wh% between the groups per breathing phase (44). The level of significance considered was  $p < .05$ .

### **3. Results**

#### **3.1 Sample's characterization**

The six long-term care facilities invited to participate in the study had in total 237 subjects: 72 older people with dementia and 165 older people without dementia. Forty two subjects with dementia were excluded as they: i) presented significant cardiac or respiratory disease and/or were prescribed with medication for the respiratory system ( $n=13$ ); ii) were talking, moving up or restless during respiratory auscultation ( $n=9$ ); iii) refused to answer to the MMSE ( $n=6$ ); iv) died during the data collection period ( $n=6$ ); v) refused auscultation ( $n=5$ ); or vi) were transferred to another care facility ( $n=3$ ). Therefore, 30 people with dementia were included in the DG. From the 165 older people without dementia, 30 were randomly assigned to the CG.

On average people were  $84.8 \pm 7.5$  years old in the dementia group and  $81.7 \pm 7.1$  years old in the control group. Most participants were female (DG:  $n=22$ ; 73.3% / CG:  $n=17$ ; 56.7%), widows (DG:  $n=16$ ; 53.3% / CG:  $n=16$ ; 53.3%) and had 1 to 4 years of education (DG:  $n=19$ ; 63.3% / CG:  $n=25$ ; 83.3%) in both groups (Table 1). There were no significant differences between the groups for those variables (Table 1).

Participants of the DG had significantly lower anthropometric values, i.e., mean waist circumference ( $p=.010$ ) and skin folds ( $p<.001$ ) than participants of the CG (Table 1).

The MMSE mean results were  $7.7 \pm 7.9$  in participants from the DG and  $24.6 \pm 5$  in participants from the CG (Table 1), meaning that, as expected, people with dementia presented high levels of cognitive impairment.

Most participants in the DG had unspecified dementia ( $n=17$ ; 56.7%), followed by Alzheimer's disease ( $n=8$ ; 26.7%), vascular dementia ( $n=4$ ; 13.3%) and dementia associated with Parkinson's disease ( $n=1$ ; 3.3%) (Table 1).

The global deterioration scale results indicated that most participants of the DG had moderately severe dementia (Table 1).

**Table 1:** Sample characteristics.

Variables	Dementia		Control		p-value
	Group (n=30)		Group (n=30)		
<b>Age</b>	84.8±7.5		81.7±7.1		0.109 <sup>a</sup>
<b>Gender</b>					0.139 <sup>b</sup>
Female	22	73.3	17	56.7	
Male	8	26.7	13	43.3	
<b>Marital Status</b>					0.110 <sup>b</sup>
Widowed	16	53.3	16	53.3	
Single	7	23.3	2	6.7	
Married/living with a partner	7	23.3	9	30.0	
Divorced/separated	0	0.0	3	10.0	
<b>Years of education</b>					0.083 <sup>b</sup>
Illiterate	8	26.7	2	6.7	
1-4	20	66.7	27	90.0	
5-9	2	6.7	1	3.3	
<b>Waist circumference</b>	92.30±14.75		101.30±11.19		<b>0.010<sup>a</sup></b>
<b>Skin folds</b>					
Triceps	7.4±3.4		9.4±3.9		<b>0.044<sup>a</sup></b>
Biceps	4.1±2.3		6.1±2.7		<b>0.004<sup>a</sup></b>
Suprailiac	7.1±2.9		10.4±4.1		<b>0.001<sup>a</sup></b>
Subscapular	6.9±3.2		10.8±3.4		<b>&lt;.001<sup>a</sup></b>
<b>Cognitive status (MMSE) (0-30)</b>	7.7±7.9		24.6±5.0		<b>&lt;.001<sup>a</sup></b>
<b>Type of dementia</b>			N/A		N/A
Unspecified dementia	17	56.7			
Alzheimer's disease	8	26.7			
Vascular dementia	4	13.3			
Dementia associated with PD	1	3.3			
<b>Severity of dementia (GDS) (0-7)</b>	6.3±0.9		N/A		N/A

Legend: Values are presented as mean ± standard deviation or prevalence and percentage. <sup>a</sup>Independent samples t-test; <sup>b</sup>Chi-square test; MMSE: mini mental state examination; GDS: global deterioration scale; N/A: not applicable; PD: Parkinson Disease; In bold statistically significant p-values:  $\alpha < 0.005$ .



## **3.2 Respiratory sounds**

### **3.2.1 Normal Respiratory sounds**

#### **3.2.1.1 Frequency**

There were no significant differences between the groups in frequency (i.e., F25, F50, F75 and Fmax.) during inspiration and expiration at both trachea and thorax (table 2).

#### **3.2.1.2 Intensity**

Subjects without dementia presented significantly higher values in I<sub>max</sub> during inspiration ( $p=0.007$ ) and expiration ( $p<0.001$ ) at trachea, than subjects with dementia (table 2). Significant differences were also found in I<sub>mean</sub> during inspiration ( $p=0.003$ ) and expiration ( $p=0.001$ ) at trachea and during inspiration ( $p=0.005$ ) and expiration ( $p=0.011$ ) at thorax. Higher values were found at trachea in people without dementia and at thorax in people with dementia (table 2).

**Table 2:** Description of the normal respiratory sound spectrum (100-2000Hz) during inspiration and expiration at trachea and thorax.

Chest			Dementia	Control	p-value <sup>a</sup>
Location			Group (n=30)	Group (n=30)	
Trachea	F <sub>25</sub> (Hz)	Inspiration	269.68 [240.88;308.61]	278.11 [248.55;316.72]	0.496
		Expiration	257.00 [214.56;304.80]	260.30 [239.54;309.90]	0.416
	F <sub>50</sub> (Hz)	Inspiration	633.08 [589.42;699.99]	666.57 [578.46;743.60]	0.237
		Expiration	625.82 [544.00;678.91]	625.24 [588.57;698.35]	0.301
	F <sub>75</sub> (Hz)	Inspiration	1134.88 [1050.13;1235.88]	1157.75 [1083.10;1236.89]	0.751
		Expiration	1105.72 [1035.91;1188.26]	1112.32 [1062.37;1191.22]	0.906
	Fmax. (Hz)	Inspiration	118.62 [102.93;213.97]	110.48 [104.34;207.40]	0.982
		Expiration	120.52 [104.96;292.84]	107.36 [102.27; 179.23]	0.092
	Imax. (dB)	Inspiration	36.88 [29.42;39.92]	39.84 [36.50;44.17]	<b>0.007</b>
		Expiration	34.51 [32.06;38.87]	42.33 [36.92;44.98]	<b>&lt;0.001</b>
	Imean (dB)	Inspiration	15.23 [12.08;18.60]	18.93 [15.64;21.82]	<b>0.003</b>
		Expiration	14.57 [12.08;18.30]	18.87 [15.64;21.44)	<b>0.001</b>
Thorax	F <sub>25</sub> (Hz)	Inspiration	213.74 [194.69;236.65]	208.58 [184.07;237.52]	0.182
		Expiration	209.26 [185.71;236.51]	204.10 [181.23;234.83]	0.317
	F <sub>50</sub> (Hz)	Inspiration	587.06 [512.54;631.53]	580.64 [512.49;640.68]	0.939
		Expiration	575.69 [513.94;637.76]	575.06 [506.15;636.46]	0.791
	F <sub>75</sub> (Hz)	Inspiration	1066.18 [985.18;1123.66]	1060.41 [986.53;1123.95]	0.739
		Expiration	1072.85 [995.65;1131.32]	1058.40 [985.90;1115.14]	0.310
	Fmax. (Hz)	Inspiration	104.96 [102.95;108.40]	104.96 [102.27;108.43]	0.849
		Expiration	103.32 [102.95;106.96]	103.35 [102.27;106.76]	0.799
	Imax. (dB)	Inspiration	49.78 [45.61;52.75]	48.93 [44.98;51.55]	0.051
		Expiration	49.30 [45.77;52.25]	48.73 [45.15;51.87]	0.183
	Imean (dB)	Inspiration	17.29 [16.04;19.31]	16.45 [15.05; 18.79]	<b>0.005</b>
		Expiration	16.71 [15.31;18.56]	16.38 [14.40;17.85]	<b>0.011</b>

Legend: Values are shown as median [interquartile range]. F<sub>25</sub>: frequency at percentile 25; F<sub>50</sub>: frequency at percentile 50; F<sub>75</sub>: frequency at percentile 75; Fmax.: frequency at maximum intensity; Imax.: maximum intensity; Imean: mean intensity; <sup>a</sup> Mann-Whitney U test; In bold statistically significant p-values:  $\alpha < 0.005$ .

### 3.2.2 Adventitious respiratory sounds

#### 3.2.2.1 Crackles

There were no significant differences between groups in crackles' mean number, frequency, IDW, 2CDs and LDW during inspiration and expiration in both trachea and thorax (Table 3).

**Table 3:** Crackles' parameters during inspiration and expiration at trachea and thorax.

Chest			Dementia	Control	p-value <sup>a</sup>
Location			Group (n=30)	Group (n=30)	
Trachea	<b>N</b>	Inspiration	0.30 [0.00-0.69]	0.31 [0.11-0.62]	0.858
		Expiration	0.38 [0.17-0.99]	0.54 [0.21-1.00]	0.620
	<b>F (Hz)</b>	Inspiration	263.78 [148.71-552.46]	249.96 [131.55-420.55]	0.468
		Expiration	322.01 [132.05-463.02]	141.07 [130.55-267.10]	0.171
	<b>IDW (ms)</b>	Inspiration	2.19 [1.25-3.56]	2.67 [2.01-3.49]	0.296
		Expiration	2.36 [1.34-4.25]	2.88 [1.66-4.41]	0.505
	<b>2CD (ms)</b>	Inspiration	7.95 [5.52-13.42]	10.86 [7.68-14.25]	0.183
		Expiration	9.65 [6.15-15.22]	13.36 [8.39-15.09]	0.393
	<b>LDW (ms)</b>	Inspiration	1.74 [0.84-2.74]	2.34 [1.71-3.11]	0.082
		Expiration	2.06 [1.52-3.07]	2.96 [2.00-3.20]	0.065
Thorax	<b>N</b>	Inspiration	1.10 [0.87-1.36]	1.10 [0.97-1.38]	0.525
		Expiration	1.71 [1.39-2.19]	1.65 [1.41-2.04]	0.882
	<b>F (Hz)</b>	Inspiration	188.64 [155.98-219.47]	159.13 [138.87-222.35]	0.124
		Expiration	190.84 [154.68-231.90]	176.34 [146.31-195.87]	0.188
	<b>IDW (ms)</b>	Inspiration	3.68 [3.51-3.85]	3.67 [3.34-4.00]	0.790
		Expiration	3.73 [3.53-3.99]	3.70 [3.52-3.92]	0.515
	<b>2CD (ms)</b>	Inspiration	13.38 [12.62-14.12]	13.89 [12.62-14.46]	0.315
		Expiration	13.42 [12.99-14.18]	13.56 [13.01-14.46]	0.802
	<b>LDW (ms)</b>	Inspiration	2.77 [2.56-3.02]	2.89 [2.78-3.05]	0.143
		Expiration	2.86 [2.72-2.94]	2.91 [2.71-2.97]	0.574

Legend: Values are shown as median [interquartile range]; N: number; F: frequency; IDW: initial deflection width; 2CD: two cycle duration; LDW: largest deflection width; <sup>a</sup> Mann-Whitney U test; In bold statistically significant p-values:  $\alpha < 0.005$ .

### 3.2.2.2 Wheezes

Groups were not significantly different in the mean number, frequency and Wh% of wheezes during inspiration and expiration in both trachea and thorax (Table 4).

Low frequency wheezes were found in both groups during inspiration and expiration.

**Table 4:** Wheezes parameters during inspiration and expiration at trachea and thorax.

Chest		Dementia	Control	p-value <sup>a</sup>
Location		Group (n=30)	Group (n=30)	
Trachea	<b>N</b>			
	Inspiration	0.05 [0.00;0.15]	0.13 [0.00;0.30]	0.218
	Expiration	0.11 [0.00;0.17]	0.06 [0.00;0.18]	0.932
	<b>Wh%</b>			
	Inspiration	1.18 [0.00;4.45]	2.62 [0.00;7.69]	0.558
	Expiration	1.81 [0.00;3.68]	1.03 [0.00;4.56]	0.823
	<b>F(Hz)</b>			
	Inspiration	410.44 [277.21;510.31]	357.30 [289.63;401.82]	0.338
	Expiration	336.96 [183.00;410.98]	375.12 [328.35;522.28]	0.119
Thorax	<b>N</b>			
	Inspiration	0.05 [0.02;0.10]	0.05 [0.02;0.13]	0.739
	Expiration	0.09 [0.03;0.33]	0.07 [0.03;0.27]	0.734
	<b>Wh%</b>			
	Inspiration	1.53 [0.52;3.71]	1.51 [0.56;3.35]	0.667
	Expiration	1.75 [0.47;5.99]	1.07 [0.49;4.50]	0.641
	<b>F(Hz)</b>			
	Inspiration	387.59 [228.08;504.37]	468.26 [269.27;597.85]	0.144
	Expiration	429.95 [273.81;606.18]	490.39 [327.73;559.91]	0.910

Legend: Values are shown as median [interquartile range] or N sum: sum of mean number; min.: minimum; max.: maximum; Wh%: occupation rate - duration of wheeze/duration of phase; F: frequency; N/A: not applicable; <sup>a</sup> Mann-Whitney U test; In bold statistically significant p-values:  $\alpha < 0.005$ .

## 4. Discussion

This study characterized computerized respiratory sounds in people with and without dementia, confirming the applicability of computerized auscultation in a non-collaborative population.

Both, people with and without dementia presented similar characteristics of normal and adventitious respiratory sounds with the exception of NRS intensity at trachea and thorax. People with dementia presented significantly lower intensity values of NRS at trachea, possibly explained by a decrease in sound generation resulting from the drop in inspiratory airflow. This

decrease could be caused by their poor cooperation, as cognitive impairment in some cases lead to misunderstanding of the request to breathe deeply and due to the common use of medicines to the central nervous system (54). These drugs could cause depression of the movements of intercostal muscles, alteration of the shape and motion of chest wall and decrease of the rib cage excursion affecting respiratory system mechanics. Therefore, in contrast with people with dementia, people without dementia presented higher intensity values of NRS at trachea suggesting higher airflows, which is in agreement with a recent study from Jácome and colleagues (18). Their study found that in people with chronic obstructive pulmonary disease the normal respiratory sound intensity also increased at higher airflows (18).

In thorax, people with dementia presented higher mean intensity values of NRS when compared with people without dementia. The authors hypothesized that these higher intensity could result from the higher effort associated with breathing in people with dementia, known as “puerile respiration” a term introduced by Laënnec as an increased sound intensity heard in adults after exertion (55). However, most of the differences between DG and CG are strictly speaking in limits of individual variability (<10%). This study does not allow us to determine if the small differences found between the groups are due to the lack of real difference or due to the small sample, which may not be sufficient to detect truly significant changes between people with and without dementia. Therefore, more studies are needed to compare findings, as very few information on standardized description and evaluation methods for normal respiratory sounds is available (14, 55).

Similar frequency values of normal respiratory sounds at trachea and thorax were found in both groups, confirming similar airflow turbulence in people with and without dementia, which was expected due to the clinical stability of participants. Moreover, the frequency values of NRS found did not suggest the presence of respiratory disease, since they were in accordance with the standard clinical characteristics of NRS, which reference values were from 100 to 5000 Hz at trachea and from 100 to 1000 Hz at thorax (11, 14). Characterizing NRS constitute an important step in the establishment of the normal respiratory sound parameters in stable older people with and without dementia, which will allow future comparisons with people presenting respiratory tract infections. Further studies are needed to investigate this issue.

People with and without dementia presented ARS (crackles and wheezes) with similar characteristics during inspiration and expiration at trachea and thorax. Therefore, crackles' number was similar in both groups, suggesting that crackles did not indicate lung pathology, agreeing with NRS findings. Two mechanisms could explain its genesis, i.e., air bubbling through secretions or the sudden opening of collapsed airways during inspiration or closing during expiration, as a result of fast pressure equalization of lung compartments (56-58). Crackles' occurrence depends on the lung volumes achieved during auscultation (57) and on properties of the lungs. Both groups were elderly and lung properties change with age, i.e., the lung elastic recoil pressure decreases at the same time that residual volumes increases, explaining the crackling sounds (59) of both groups.

Most crackles presented longer durations and low frequencies suggesting the presence of coarse crackles in both groups (39, 40), that are consistent with the presence of sputum in proximal airways (20, 60). This finding could be explained by the common low forced expiratory flow rates and lower lung elastic recoil at an advanced age (57), which reduce the efficacy of airway secretions clearance by coughing (61, 62) and leads to an accumulation in proximal airways. Therefore, crackles assessment is essential, to contribute for estimating the presence and location of secretions (15). It can also contribute for the differential diagnosis of respiratory diseases, as their number relates with the severity of the disease and their waveform and positioning within the respiratory cycle are characteristics to differentiate lung pathological cases (15).

Following our previous findings of NRS and crackles, no significant differences in the number and frequency of wheezes were found between groups, which suggests that participants from both groups did not have airway obstruction or presented a flow limitation that interferes with the flutter mechanism required to produce wheezes (14, 61). Additionally, a low occupation rate was found in both people with and without dementia, meaning that a small percentage of the respiratory cycle was occupied by wheezes. This suggests a reduced airway obstruction at proximal airways possibly due to the secretions movement (14), but consistent with the absence of respiratory disease. This absence among the two groups is an important clinical finding, as wheezes are considered one of the most easily recognized adventitious respiratory sound (11) and their presence is an important indicator of the respiratory system status which also complements the crackles' assessment.

Although previous studies stated that differences in anthropometric values influenced adventitious respiratory sounds characteristics (63, 64), this was not supported by our findings, which deserves further investigation.

Finally, it is known that age affects lung volumes and capacities, due to some degree of physiological degeneration of the respiratory system, reduced mucociliary function and lower flow rates (62). This study suggested a decrease in airflow, accompanied by a great effort to breathe in people with dementia, based on the characteristics of NRS. These alterations along with the low anthropometric values and poor mobility found in subjects with dementia may represent great difficulty in overcoming future respiratory disease, explaining their higher rates of hospitalization (5), longer periods in the hospital (65) and higher mortality (2). However, these findings should be considered with caution, due to the exploratory nature of this study. Therefore, NRS and ARS routine assessment and analysis through computerized auscultation demonstrate potential to obtain relevant clinical information about the respiratory system. This could allow prevention, early diagnosis and continuous monitoring of LRTIs, mainly in non-collaborative populations, in different settings.

#### **4.1 Limitations and future research**

The relative small sample size included in this study limits the generalization of the findings. Larger samples will strengthen these results. Moreover, the sample size used may not be

sufficient to detect truly significant changes between older people and people with dementia (type II error). Studies with sample size estimations are also needed. Therefore, this exploratory study is a first step towards the use of computerized respiratory sounds in the objective assessment of people with dementia and could be used as a pilot study to compute sample sizes in future studies.

In this study only one recording per chest location was performed as people with dementia are extremely restless and agitated. The inability to collect 3 measurements at each respiratory system site did not allow reliability assessment, which would have strengthened our findings. However, previous studies (20, 66) have demonstrated excellent intra-subject reliability and validity of computerized respiratory sounds.

The lack of airflow assessment simultaneously with respiratory sounds also limited our findings, as respiratory sound generation is affected by lung volume and airflow (21, 67). However the cognitive impairment presented by people with dementia broadly restricted their collaboration in data collection, and in most cases it will be nearly impossible to take them to breath by a mouth piece, while the researcher/clinician perform auscultation.

Finally, studies including 3 groups (people with dementia vs. people with dementia presenting a respiratory infection vs. matched people without dementia) could be interesting to further enhance knowledge on the respiratory system and inform health promotion and prevention of respiratory infections.

## **5. Conclusion**

People with and without dementia had similar characteristics of normal and adventitious respiratory sounds, with the exception of NRS intensity. People with dementia presented lower intensity values at trachea and higher intensity values at thorax.

Although people with dementia have extreme difficulties to participate in the diagnosis and treatment of respiratory diseases, it was possible to collect and study their respiratory sounds, due to the non-invasive nature of computerized auscultation and the minimal need for collaboration. Moreover, the recording of computerized respiratory sounds in people with dementia stable, without respiratory disease, could be the step towards prevention, early diagnosis and continuous monitoring of respiratory diseases or exacerbations states in different settings.

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